A STUDY ON TYPES OF ANEMIA IN PATIENTS WITH CHRONIC RENAL INSUFFICIENCY IN BUNDELKHAND REGION

&

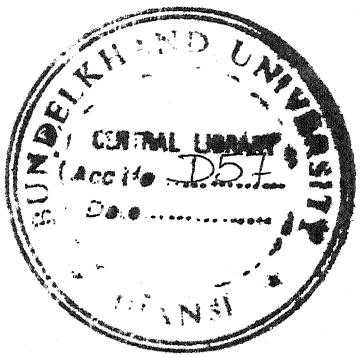
A COMPARATIVE STUDY OF ORAL VS INTRAVENOUS IRON THERAPY IN PATIENTS WITH CHRONIC RENAL INSUFFICIENCY

THESIS

FOR

DOCTOR OF MEDICINE

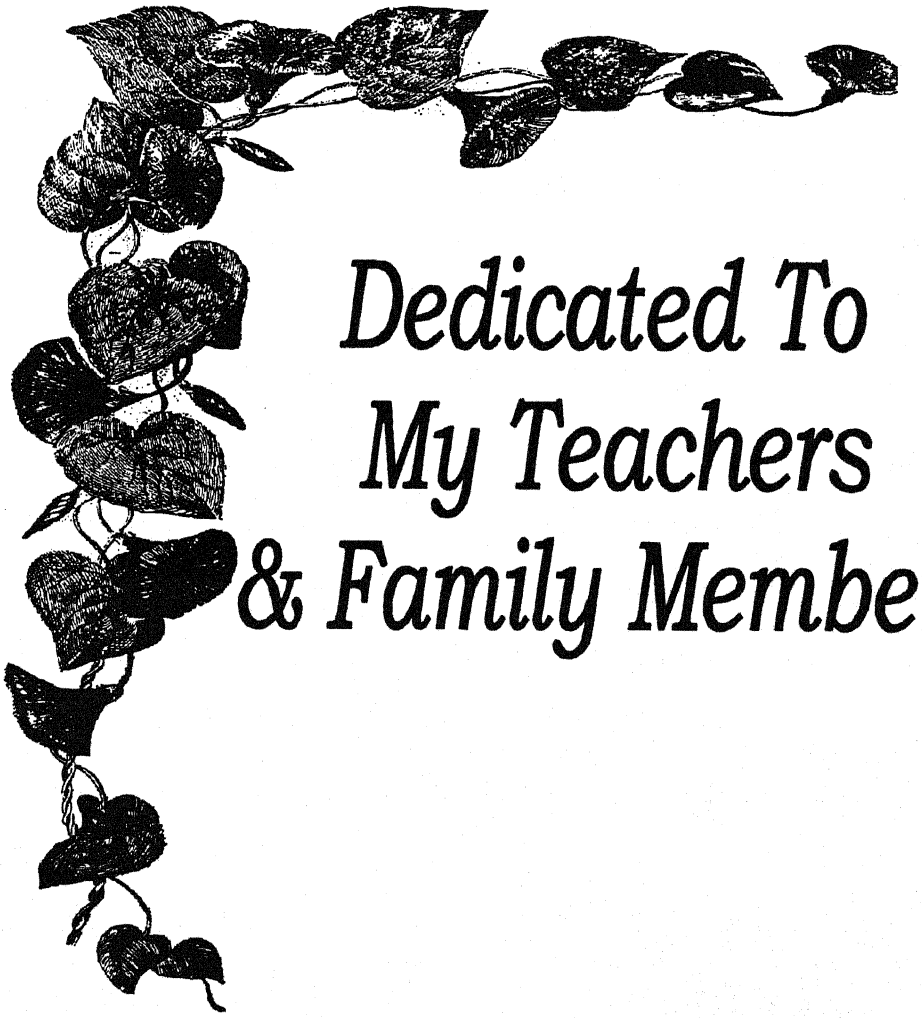
(INTERNAL MEDICINE)



BUNDELKHAND UNIVERSITY
JHANSI (U.P.)

2007

SHAILESH KUMAR SRIVASTAVA



Dedicated To
My Teachers
& Family Members

DEPARTMENT OF MEDICINE

M.L.B. Medical College, Jhansi (U.P.)

CERTIFICATE

This is to certify that the work entitled "***A study on types of anemia in patients with chronic renal insufficiency in Bundelkhand region and a comparative study of oral vs intravenous Iron therapy in patients with chronic renal insufficiency***" which is being submitted as thesis for M.D. (Medicine) Examination 2007 of the Bundelkhand University, Jhansi, has been carried out by **Dr. Shailesh Kumar Srivastava** in the department of Medicine, M.L.B. Medical College, Jhansi.

The method described was undertaken by the candidate himself and the observations recorded were periodically checked. He has put in the necessary stay in the department as per University regulations, and has fulfilled the conditions required for the submission of thesis according to University regulations.

Dated:

Place - Jhansi

Prof. P.K. Jain
M.D., MNAMS
Professor & Head,
Department of Medicine,
M.L.B. Medical College,
Jhansi (U.P.)

DEPARTMENT OF MEDICINE

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Dated:

Place - Jhansi

Dr. N.S. Sengar
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Jhansi (U.P.)
(GUIDE)

DEPARTMENT OF MEDICINE

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Dated:

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Dr. D. Nath
M.D.
Associate Professor,
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(CO-GUIDE)

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Last but not the least, I pay my sincere thanks to all my patients who were the very basis of this study.

Date : 29/12/06

Dr. Shailesh Kumar Srivastava

CONTENTS

Introduction

INTRODUCTION

Chronic renal disease (CRD) has been defined as a pathophysiologic process with multiple etiologies, resulting in the inexorable attrition of nephron number and function and frequently leading to end stage renal disease (ESRD). ESRD represents a clinical state or condition in which there has been irreversible loss of endogenous renal function, of a degree sufficient to render the patient permanently dependent upon renal replacement therapy in order to avoid life threatening uremia. The pathophysiologic process must last for more than 3 months in order to make the diagnosis of CRD.

CRD has been graded into five different stages, based on glomerular filtration rate –

STAGES OF CHRONIC RENAL DISEASE :

Stage	Description	GFR (ml/min per 1.73m^2)
	At increased risk	90 (with risk factors)
1	Kidney damage with normal or increased GFR	90
2	Kidney damage with mildly decreased GFR	60-89
3	Moderately decreased GFR	30-59
4	Severely decreased GFR	15-29
5	Renal failure	<15 (or dialysis)

HAEMATOLOGIAL DISORDERS IN CRD

The close relationship between haematopoiesis and the kidney was first recognized by Richard Bright in 1836 when he described the association between anemia and chronic renal failure (CRF).

A lot of progress has been made in this field since then, in order to understand the relationship between anemia and CRD and now it is well established that much of the morbidity in renal failure patients is because of the consequences of their chronic anemia. Disorders of white cell and platelet function have also been described in renal failure, but these are of secondary importance compared with those related to the red cell.

PATHOPHYSIOLOGY OF ANEMIA IN CKD

Anemia begins to develop as the GFR falls below 60ml/mt, and Hb typically falls below 11gm/dl as the GFR drops below 30ml/mt. Patients with diabetes and CKD tend to develop anemia earlier and to a greater degree than patients without diabetes.

FACTORS CONTRIBUTING TO DEVELOPMENT OF ANEMIA IN CKD

The major determinant of renal anemia is depressed erythropoiesis which is primarily due to relative erythropoietin (Epo) deficiency.

Various other factors that contribute to development of renal anemia include –

- Reduced red cell life span
- Iron deficiency

- Folate and B_{12} deficiency
- Aluminium toxicity
- Marrow fibrosis resulting from hyper-parathyroidism
- Role of uremic inhibitors of erythropoiesis in development of renal anemia is still controversial and is under investigation.

Besides there are certain other factors that also play a role in development of renal anemia-

- Stress ulceration that can lead to substantial GI blood loss.
- Proton pump inhibitors, commonly prescribed in CKD to treat stress ulceration reduce iron absorption form GIT.
- Modified diets intended to reduce phosphate or protein in CKD also affect levels of dietary iron.
- Uremia leads to anorexia and nausea which further reduces intake and absorption of iron.
- Calcium binders also reduce iron absorption from gut.
- Blood loss due to hemodialysis
- Over zealous blood sampling

TYPES OF ANEMIA IN CKD

The peripheral blood film in a patient with CKD classically reveals a normocytic normochronic picture, occasionally with fragmented red cells or burr cells. The reticulocyte count is low for the degree of anemia and the white cell count is usually normal. There may be reduced, normal or

increased cellularity of bone marrow and the myeloid erythroid ratio may be decreased. There is a reduced red cell mass, but normal total blood volume except in patients who are fluid over loaded.

However, at times, the blood picture may be different from this typical presentation, being more in favour of microcytic hypochronic or macrocytic smear suggesting the predominant role of iron deficiency or B_{12}/Folate deficiency in causation of anemia, respectively.

IRON DEFICIENCY IN CKD

In developing countries like India, the commonest cause of iron deficiency, apart from increased requirement, are poor availability of iron in the predominant vegetarian diets and increased loses due to parasitic infestations (Park and Park). Mehta (1990) reported that dietary deficiency due to poverty, faulty food habits due to religious beliefs or other reasons, food fads and faulty cooking habits were the commonest factors contributing to iron deficiency and anemia. As the iron deficiency anemia is very wide spread in our country, it maybe a major contributory factor towards the anemia of CKD.

Besides, when the patients of CKD are put on erythropoietin (Epo) therapy, the rate of erythropoiesis is increased substantially, thus imposing significantly increased iron requirements. If the marrow stores are inadequate or the patients are not given iron concurrently, a state of functional iron deficiency in created leading to a picture of iron deficiency anemia. Therefore it is recommended that patient's iron stores should be well repleted before starting Epo therapy and a maintenance dose of iron be continued during Epo therapy, keeping a watch on iron status of the patient.

ASSESSMENT OF IRON STATUS

There are four basic measurements that reflect the iron status of body. These are :-

- **Serum iron level** – Reflects the level of circulating iron
- **Serum ferritin level** – Reflects the stored iron in the reticuloendothelial cells of bone marrow, spleen and liver or in the parenchymal cells of the liver.
- **Percentage saturation of transferrin [TSAT]** – Transferrin is an iron binding protein in the blood which transports iron through the plasma and extravascular space. Normal saturation of transferring with iron is 30-50%.
- **Total iron binding capacity [TIBC]** – Reflects transferrin's ability to bind iron. It represents the total amount of iron that can bind to transferrin to give 100% saturation of the binding sites.

TIBC is increased in iron deficiency and decreased in iron over load.

These are the best indicator of iron available for erythropoiesis and iron stores, but they do not provide absolute criteria for either iron deficiency or iron overload.

MANAGEMENT OF IRON DEFICIENCY IN CKD

National Kidney foundation – Kidney Disease /Dialysis outcome quality initiative (NKF-K/DOQI) Guidelines 2000 (Revised in 2005)

NKF-K/DOQI provides certain guidelines for optimal management of iron deficiency in CKD patients :

- Assessment of iron status – Iron status should be assessed by serum ferritin and percent saturation of transferrin (TSAT).
- Target iron level
  - CKD patients should have sufficient iron to achieve and maintain a hemoglobin (Hb) of 11-12 gm/dl and a hematocrit (Hct) of 33% to 36%.
  - To achieve and maintain this target Hb/Hct, sufficient iron should be administered to maintain a TSAT of ≥20% and a serum ferritin level of ≥ 100ng/dl.
- Monitoring iron status
  - During initiation of Epo therapy and while increasing the Epo dose, in order to achieve an increase in Hb/Hct, the TSAT and the serum ferritin should be checked every month in patients not receiving I/V iron, and atleast once every 3 months in patients receiving I/V iron, until target Hb/Hct is achieved.
  - Following attainment of the target Hb/Hct, TSAT and serum ferritin should be determined at least once every 3 months.

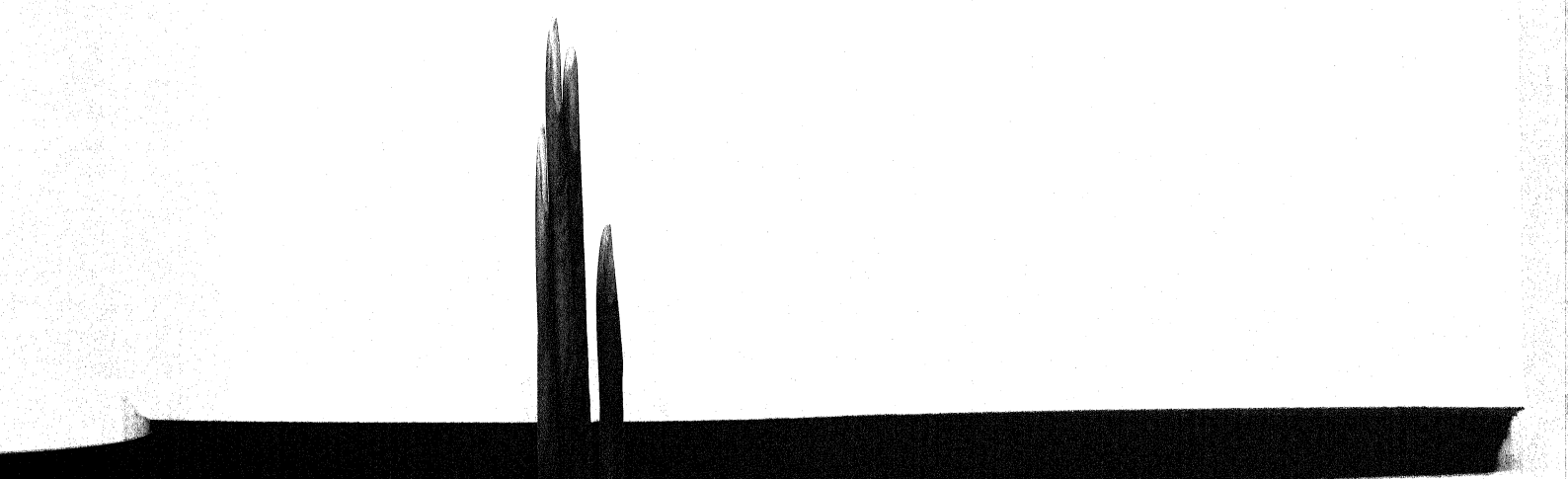
- Administration of supplemental iron
  - Supplemental iron should be administered to prevent iron deficiency and to maintain iron stores so that CKD patients can achieve and maintain a Hb of 11 to12 gm/dl and Hct of 33 to36 % in conjunction with Epo therapy.
  - If oral iron is given, it should be administered at a daily dose of at least 200mg of elemental iron for adults and 2 to 3 mg/dl for pediatric patients.
  - The adult CKD home hemodialysis and peritoneal dialysis patients may not be able to maintain adequate iron status with oral iron. These patients need to be put on I.V iron therapy.
  - A trial of iron is acceptable in the hemodialysis patients, but is unlikely to maintain TSAT ≥20%, se ferritin ≥ 100ng/ml and Hb/Hct at 11-12/33-36%.
  - To achieve and maintain a Hb of11-12% and Hct of 33-36%, most hemodialysis patients will require I.V iron on a regular basis.
  - I/V iron can be administered on a variety of dosage schedule depending upon the iron requirement of the patient and the preparation used.
  - Most patients will achieve target Hb and Hct with TSAT and serum ferritin level <50% and <800ng/ml respectively. In patients in whom TSAT is ≥50% and /or serum ferritin is ≥ 800ng/ml, IV iron should be withheld for up to 3 months., at which time the iron parameters should be re-measured before I/V iron is

resumed. When TSAT and serum ferritin have fallen to >50% and <800 ng/dl respectively, I/V iron can be resumed weakly at a dose reduced by one third to one half.

- It is anticipated that once the target Hb/Hct levels and iron stores are achieved, the goal is to provide a weakly dose I/V iron that will allow the patient to maintain the target Hb/Hct at a safe stable iron level. The maintenance iron status should be monitored by measuring the TSAT and serum ferritin no less than every 3 months.

- Oral iron is not indicated for the CKD patients who requires maintenance doses of I/V iron.

Aims & Objectives



AIMS AND OBJECTIVES

1. To study the type of anemia in patients with chronic renal insufficiency.

2. To compare the response of oral therapy with intravenous iron therapy in terms of improvement in hematological parameters in patients with chronic renal insufficiency.

INCLUSION AND EXCLUSION CRITERIA

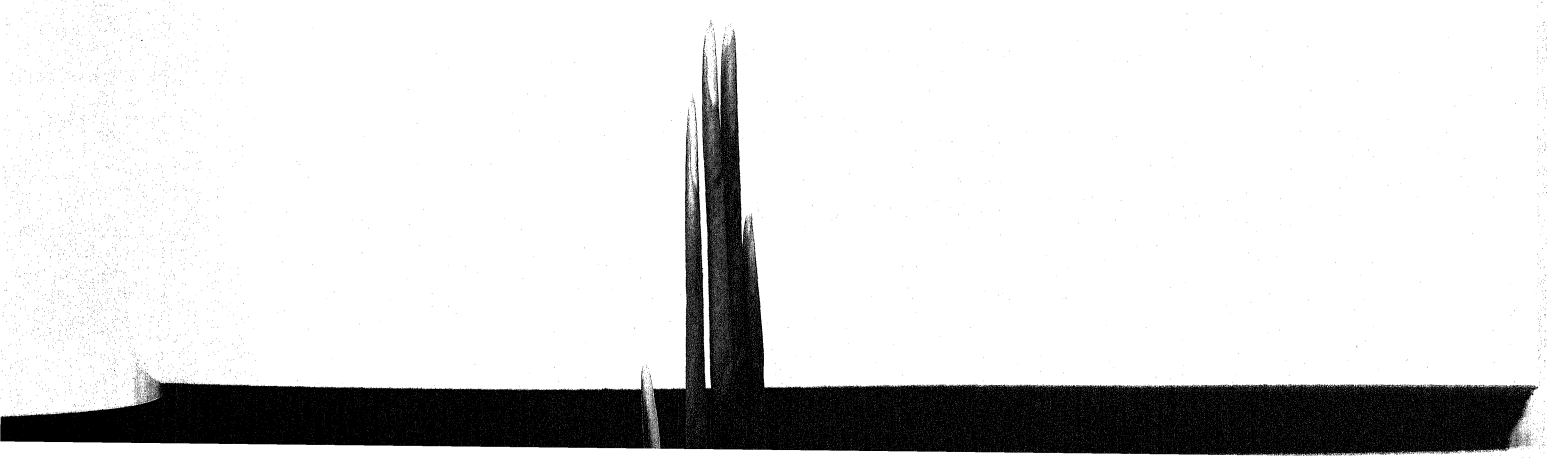
Inclusion criteria

1. Age 15 years and above
2. Established cases of chronic renal failure and anemia.

Exclusion criteria

1. Presence of any associated bleeding disorder.
2. Presence of chronic inflammatory disease e.g rheumatoid arthritis, chronic hepatitis and TB etc.
3. Pregnancy
4. Patients on androgen therapy with in last 4 weeks.

Review of Literature



REVIEW OF LITERATURE

HISTORICAL PERSPECTIVE

It was ***Morgani (1682-1771)*** who first of all noticed hematological derangements in association with kidney disease and described the case of a person who had odour of urine on the breath and suffered form episodes and hematemasis.

The relationship between hematopoiesis and kidney was first recognized in 1836 by a British Physician ***Richard Bright***, who noted that patients with renal disease exhibited marked pallor.

In 1907, ***Riesman*** documented the hemorrhagic diasthesis in relation to renal disease and cited the original description of Morgagni.

Brown and Roth in 1992 concluded that the anemia of chronic nephritis was due to decreased bone marrow production.

Parson et al in 1993, said that the anemia in patient with kidney disease bore a direct relationship to the degree of nitrogen retention.

In 1938, ***Magner*** concluded that anemia occurs regularly in cases of renal insufficiency and nitrogen retention, regardless of the nature of the renal lesion and degree of anemia is usually proportional to the degree of impairment of the excretory functions of the kidney.

Emerson and Burrows, in 1949, demonstrated increased destruction of erythrocytes in renal failure. They also stated that uremic sera contained one or more substances that interfered with either the growth of erythroid

precursors or with heme synthesis in tissue culture, supporting the concept that uremic suppression of erythropoises is a cause of anemia of renal failure.

In 1957, ***Jacobson and coworkers*** demonstrated that the kidney was the responsible organ for the control of red cell production.

"Haematopoietene" as the substance produced bykidney that regulates red cell production was first recognized many decades back and this Haematopoietene was eventually defined as an "erythropoiesis stimulating factor by ***Erslin*** in 1953 and shortly thereafter, it was named "erythropoietin".

RECENT STUDIES

A lot of work has been done, since the era of Morgagni, in this field, in order to understand the mechanism, as well as the consequences of renal anemia. Although still not fully understood, many aspects of anemia in CKD are now becoming clear. Management of anemia in CKD patients has always been a challenging issue for practitioners. Many studies have been carried out and some are ongoing to explore the unclear aspects of anemia in CKD patients.

Bickford AK (2002), *Fresnius Medical Care, Central Dupage Dialysis Center, USA*, worked on 'Evaluation and Treatment of Iron Deficiency in Patient with kidney Disease' and found that serum ferritin and percent transferrin saturation, which are regarded as the best indicators of iron status, lack sensitivity and specificity to identify functional iron

deficiency, which can occur in the presence of normal or even increased iron stores.

Firshbane S and coworkers, *Winthrop University Hospital, Division of Nephrology, Newyork, USA* studied on 'Evaluation of Iron status In Hemodalysis patients ,' They found that a novel assay, the reticulocyte hyemogobin content (CHr) sensitively detects functional iron deficiency. They evaluated the CHr in assessment of iron status in 164 hemodialysis patients and concluded that –

- CHr is an accurate measure of iron status in hemodialysis patients.
- A reticulocyte hemoglobin content (CHr) value less than mature red cell hemoglobin content (CH) value indicates acute onset iron deficiency.
- A single dose infusion of IV iron results in correction of iron deficiency at the level of reticulocyte within 48 hours.

Bhandari S and Coworkers, *Renal unit leeds General Infirmary UK,* evaluated the role of RBC ferritin and reticulocyute hemoglobin content in monitoring the response to IV iron therapy. They conducted their study on 22 hemodialysis patients and concluded that these measurements provide evidence of increased iron supply for erythropoiesis during I.V iron therapy, help identify patients with functional iron deficiency, and allow more accurate monitoring of response to I/V iron therapy.

Seiler S (2000), *Adam Linton Dialysis Unit London Health Sciences Centre, London,* discussed newer treatment alternatives in the management of anemia of CRF. He suggested an alternate form of I/.V iron, sodium ferric gluconate, to be safe and effective in the management of iron deficiency anemia in hemodialyis patients receiving erythropoietin. He also pointed out that hemodialysis patients with serum ferritin below 100ng/ml or TSAT below 20% need supplementation with parenteral iron in excess of 1000mg to achieve optimal response in Hb/Hct levels, as suggested by US NKF-DOQI clinical practice Guidelines.

Svara F et al (1996) worked on iron supplementation during erythropoietin therapy in patients on hemodialysis. They performed a comparative study on oral vs I.V iron supplementation in the treatment of secondary anemia by recombinant human erythropoietin in patient with CKD treated by hemodialysis. The study was performed on 61 patients divided into two groups of which one group received oral iron and the other group I/V iron.

After six weeks of treatment they found that –

- Rise in Hct and Se iron were comparable in both groups.
- TSAT showed a more marked increment in I.V treated group.
- S. ferritin levels declined in oral supplementation group where as increased in I.V treated group.

Thus the study conducted by these workers suggested that although the rise in Hct and serum iron may be comparable in the patients treated with oral or I/V iron, building of iron stores is much better with I/V iron and therefore from long term aspect, the study favoured the use of I/V iron supplementation in hemodialyzed patients treated with erythropoietin.

The response to oral and I/V iron supplementation in management of anemia in CKD was also discussed by ***Macdougall IC (1999)***, *department of Renal Medicine, King's College Hospital, London (UK)* : He stressed that the need of I/V iron supplementation should be strongly considered when the serum ferritin level is <100µg/L or transferrin saturation is <20% or the percentage of hypochromic red cells is >10%. He also mentioned that when I.V iron suppelementation is given care should be taken to prevent serum ferritin rising above 800µg/L and transferrin saturation above 50% in order to avoid iron overload.

Silverberg DS and Co-workers (1999), *Department of Nephrology, Tel Aviv Medical Center, Israel* evaluated the response to I.V iron for the treatment of predialysis anemia. They found that anemia in CKD patients in the predialysis period can be improved by I/V iron to a much greater extent as compared to oral iron. In addition, the advantage of maintaining adequate iron stores with I/V iron is that, when erythropoietin is needed, lower doses will be required to achieve the target Hct than if Epo were used alone.

They also claimed an I/V iron preparation, Ferric hydroxide sucrose complex, to be extremely safe with regard to the risk of anaphylactic reactions, as the authors did not see even a single anaphylactic reaction in over 20,000 infusions over a four year period.

Nissenson AR and co-workers (1999), *University of California at Los Angeles Medical Center, USA*, evaluated the response of I/V iron, sodium ferric gluconate complex in sucrose, in anemic CKD patients on hemodialysis and found it to be highly safe an effective in improving Hb, Hct, Iron saturation and serum ferritin level.

Faich G and Strobos J (1999), *Pharmaceutical safety Assessments, Narberth, USA* also assessed the safety profile of I/V iron, sodium ferric gluconate complex in sucrose and found it to be a much better alternative I/V iron preparation as compared with iron dextrans.

Ahsan N (1998) *Department of Medicine, Milton S Hershey Medical Centre Pennsylvania state University College of Medicine, USA*, performed a comparative study on I/V vs Oral iron administration in treatment of anemia in peritoneal dialysis (PD) patients. The study was performed on 25 stable PD patients, divided into two groups, one group receiving single I/V infusion of total dose iron given on out patient basis where as the other group receiving oral iron. The study conclusively showed that the I/V iron treatment is more efficacious method of iron supplementation that oral iron in PD patients. The study also showed that

single I/V infusion of total dose iron is a safe and well tolerated method of iron administration that can be used on out patient basis.

Canavese C and coworkers (2004) *Department of Internal medicine, Section of Nephrology, University of Torino, Italy* worked on low dose continuous iron therapy in chronic hemodialysis patients. Their study included 30 chronic hemodialysis patients who were put on low dose continuous iron therapy in the form of I.V iron gluconate 31.25 mg/wk for a period of 12 month followed by a 6 month withdrawal period and then again on same dose for 9 months. The study showed a significant increased in serum ferritin and TSAT during period 1 and 3. Another important observation made in the study was serum transferring level that showed a significant decrease during period 1 and 3 while increase during period 2 (i.e. negatively correlated with ferritin). Thus, this study concluded that even low dose maintenance iron therapy with only 31.25 mg weekly over one year cannot prevent the risk of iron overload in patients with moderate anemia.

Another study published this year [Jan 2006] by ***Mircescu G et al****, Dr Carol Davila Teaching hospital of Nephrology, Romania,* evaluated the response of I.V iron sucrose for the treatment of anemia in pre-dialysis chronic renal failure patients, who were not receiving erythropoietin. This study included 60 patients who were given 200mg of elemental iron in the form of iron sucrose preparation for a period of 12 months. The study showed a significant increase in Hb, serum iron, serum ferritin and

transferrin saturation with no worsening of renal function, no increase in blood pressure and no other side effects.

The study concluded that -

- I/V Iron therapy in pre-dialysis CKD patients not receiving erythropoietin seems to ameliorates the anemia, avoiding the necessity of erythropoietin or blood transfusion in atleast one third of patients.
- I/V iron supplementation in the form of iron sucrose appears to be effective and safe for treatment of anemia in CKD patients.

Verma PP and co-workers *(July 1999) and R&R Hospital New Delhi,* studied the types of anemia in patients with CKD and role of aluminium in hypochromic anemia of CKD. Their study was performed on 64 dialysis dependent patients of CKD with adequate dietary intake (>1500cal/day) and no apparent source of blood loss and the patients were evaluated for type of anemia. The classical normocytic normochromic picture was observed in 28.5% cases, while rest had hypochromic picture. On bone marrow study two patients had zero iron stores while all other had normal or excessive iron stores. In 10 patients with hypochromic picture, mean serum aluminium level was 170μg/lit.

This study highlights the high prevalence of hypochromic anemia in patients with adequate dietary intake and aluminium overload in Indian CRF patients.

Singh NP and Co-workers, *Department of Medicine, Maulana Azad Medical College, and Associated Lok Nayak Hospitals, New Delihi* assessed the efficacy of low dose erythrpoietin therapy in treatment of anemia of CRF, and concluded that low dose erythropoietin (40U/Kg, biweekly) therapy is safe and effective in management of anemia of CRF.

Agarwal HK and Co-workers (2002) *Department of Medicine, Nephrology and Clinical Pathology, Pt. B.D. Sharma Post Graduate Institute of Medical Sciences, Rohtak (Haryana) India,* performed a comparative study on use of oral and I/V iron in predialysis patients of CRF receiving recombinant human erythropoietin.

Their study was performed on 40 adult patients of CRF, who were divided into two groups – one group receiving oral iron in the form of ferrous sulphate 200mg three times a day and another group receiving 100mg of elemental iron in the form of 2ml iron dextran, twice a month intravenously. Both the groups received recombinant human erythropoietin in the dosage of 2000 units subcutaneously twice a week. The patients were followed for a period of 3 months. From the study it was concluded that I/V iron is far better than oral iron for treatment of anemia in CRF patients receiving erythropoietin, as shown by a significant rise in hematological parameters in I.V treated group as compared with oral group.

Material & Methods

MATERIAL AND METHODS

MATERIAL

The cases for the present study were selected form the OPD and wards of Department of Medicine, M.L.B. Medical College and Hospital, Jhansi.

METHODS

The study was performed on fourty adult patients of established chronic kidney disease with anemia.

After inclusion of patients a detailed history and physical examination were performed and all the necessary baseline investigations were done to establish baseline haematological parameters. From these results the type of anemia was established in every patient. Now these patients were put randomly into two groups.

Group A – Patients of Group A received oral Iron therapy in the form of one capsule of 300mg of Ferrous fumerate (Containing 100mg of elemental iron) twice daily.

Group B – Patients of Group B received I/V iron in the form of 100mg of elemental Iron as Iron sucrose every weekly.

Patients of both the groups received recombinant human erythropoietin in the dosage of 2000units subcutaneously twice a week. Patients of both groups were followed for a patients of 3 months and at the end of study hematological parameters were reassessed. The response to iron therapy

was judged in terms of improvement in hematological parameters and the two groups were compared with each other.

ANALYSIS OF RESULTS

Data from 20 patients in each group A and B were subjected to statistical analysis. The continuous variables were recorded as means with standard deviations. In comparison between the data of same group, paired 't' test was applied whereas for comparison between two groups unpaired 't' test was applied. Paired and unpaired p values were calculated.

Observations

OBSERVATIONS

Fourty adult patients of chronic kidney disease with anemia, attending the OPD and wards of department of Medicine, Maharani Laxmi Bai medical College, Jhansi were enrolled in the present study.

After a detailed history taking and thorough physical examination, the necessary base line investigations were carried out to establish baseline hematological and renal parameters and from these nature of anemia was established. Now these patients were randomly put into two groups A and B. The patients of group A received oral iron therapy whereas patients of group B received I/V iron. Patients of both the groups were given erythropoietin in similar doses. These patients were followed upto a period of 3 months and the hematological parameters were reevaluated. The effect of oral and I/V was compared in terms of improvement in hematological parameters at the end of 3 months of therapy.

TABLE -1

Age wise distribution of patients in Group A and B

Age (yrs)	Group A		Group B	
	No.	%	No.	%
20-29	6	30.0	5	25.0
30-39	6	30.0	7	35.0
40-49	5	25.0	4	20.0
50-59	0	0	2	10.0
60-69	3	15.0	2	10.0
Range	23-66 yrs		24-68 yrs	

The age range of patients in group A was 23-66 yrs and in group B was 24-68 yrs. In group A 85% of the patients were in age group of 20-49 yrs whereas in group B 80%f the patient were in age group 20-49 yrs.

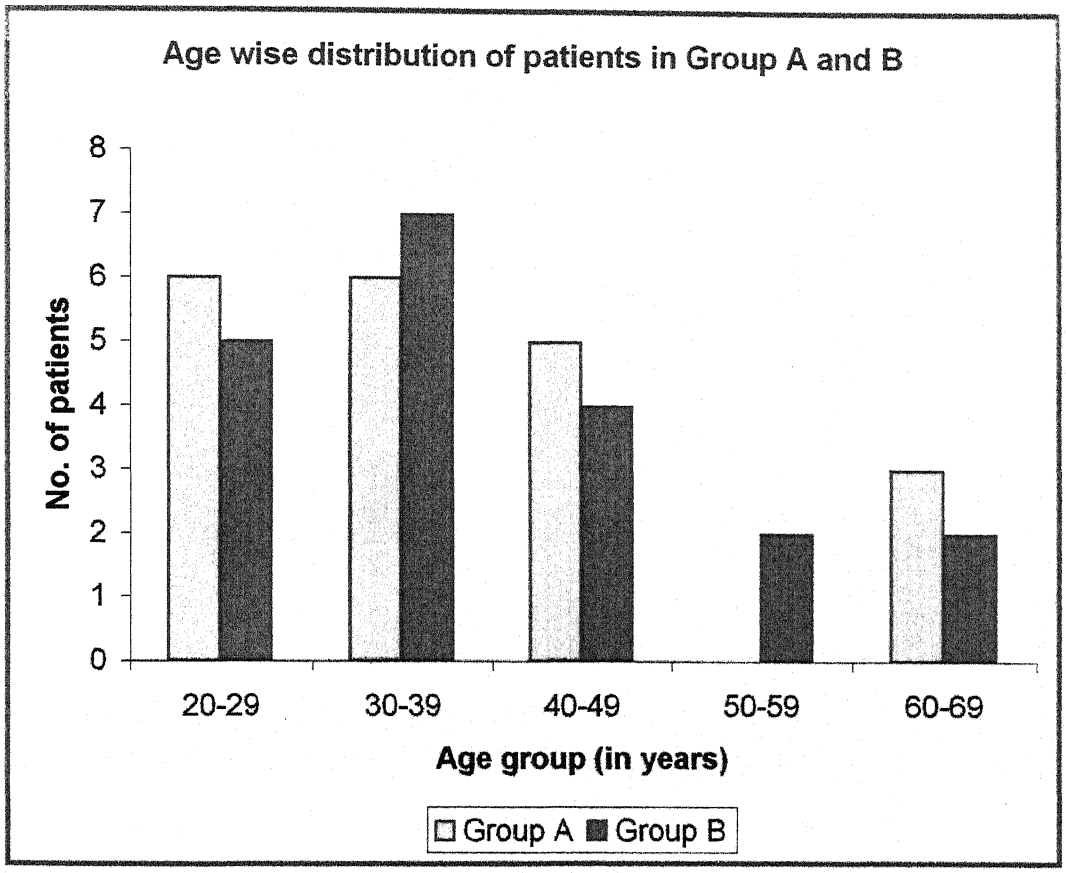

Age wise distribution of patients in Group A and B
No. of patients
0
1
2
3
4
5
6
7
8
20-29
30-39
40-49
50-59
60-69
Age group (in years)
Group A
Group B

TABLE – 2

Sex wise distribution of patients in Group A and B

Group	Male	Female	Ratio
A	13	7	1.85:1
B	15	5	3:1

In group A 13 patients were male and 7 were female with a male : female ratio of 1.8:1, whereas in group B 15 patients were male and 5 were female with a ratio of 3:1.

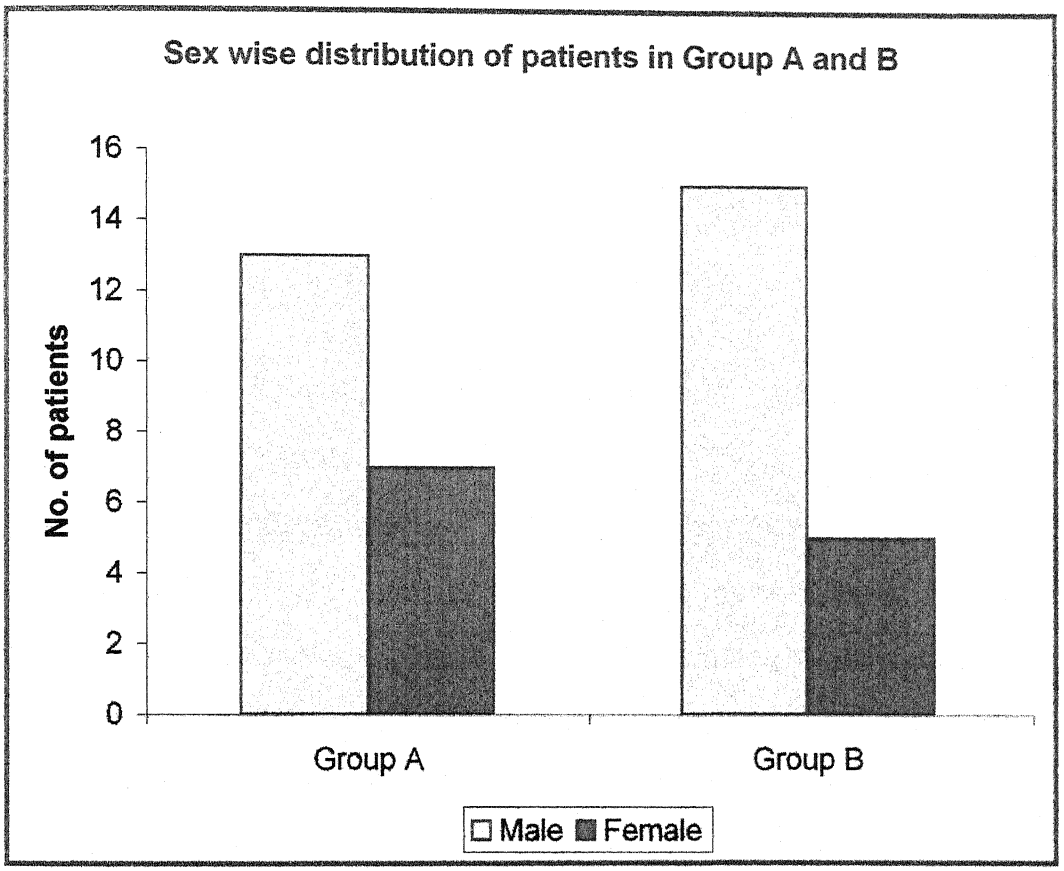

Sex wise distribution of patients in Group A and B
No. of patients
16
14
12
10
8
6
4
2
0
Group A
Group B
Male
Female

TABLE – 3

Types of anemia and their relative preponderance among all the patients studied

Types of anemia	Number of patients	Percentage
Normocytic normochronic (NN)	19	47.5
Microcytic hypochronic (MH)	13	32.5
Megaloblastic (MB)	2	5.0
Mixed	6	15.0
Total	40	

Out of all the 40 patients studied, 19 patients (amounting to 47.5%) showed characteristics consistent with the diagnosis of normocytic normochronic anemia whereas 13 patients (amounting to 32.5%) had microcytic hypochronic anemia. Two patients (amounting to 5% of all) had megaloblastic blood picture, whereas remaining 6 patients (15% of the total) showed a mixed type of morphology, not consistent with any single type of anemia.

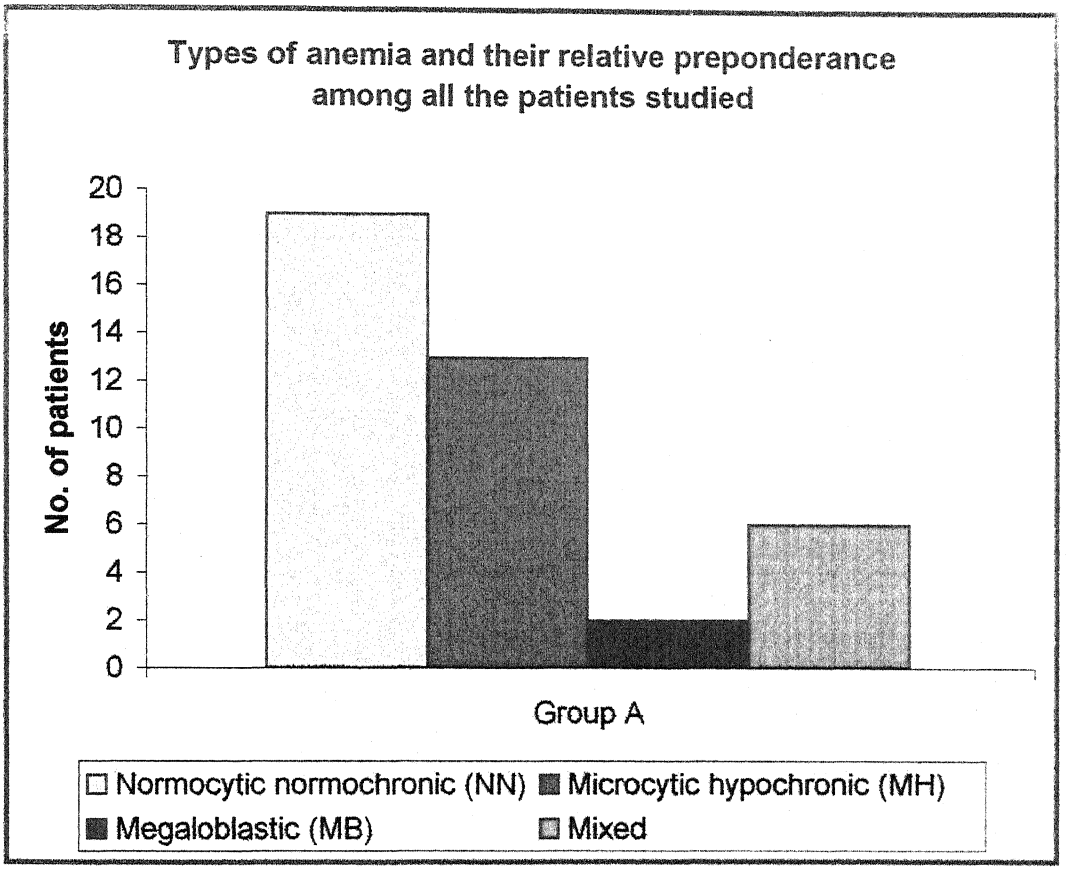
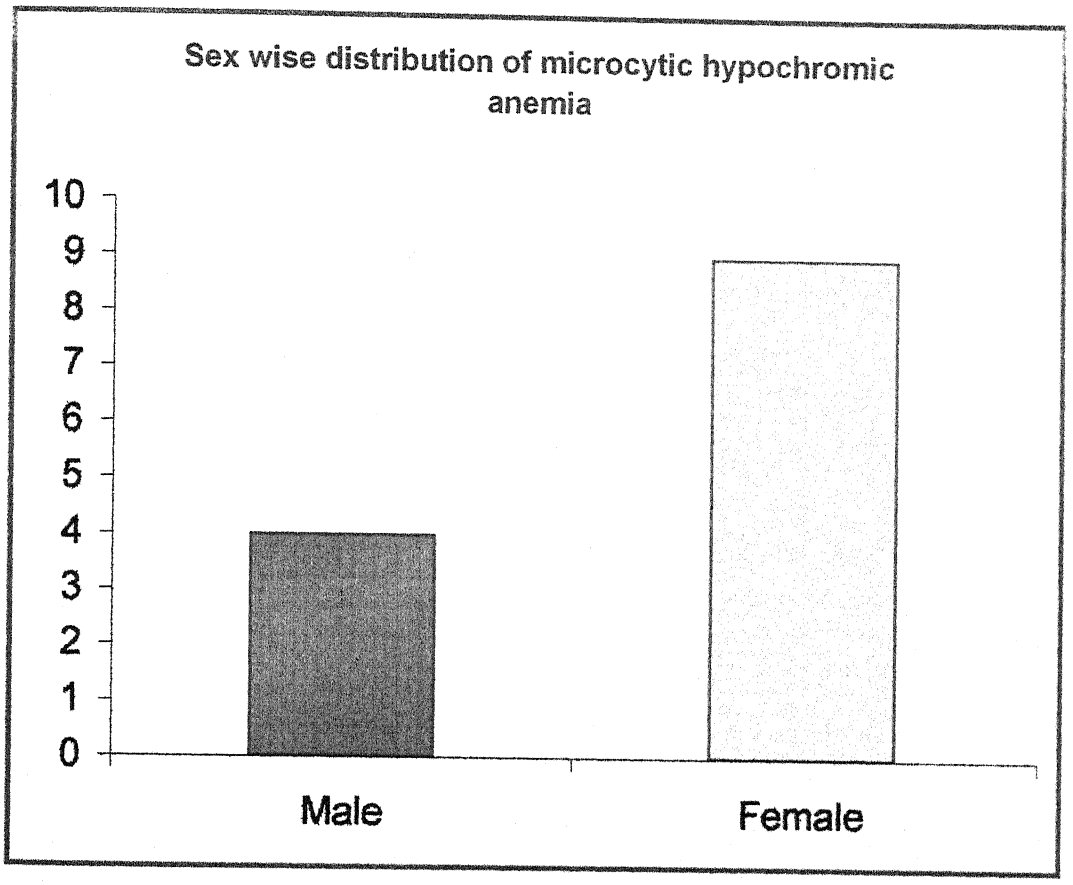

Types of anemia and their relative preponderance among all the patients studied
No. of patients
20
18
16
14
12
10
8
6
4
2
0
Group A
Normocytic normochronic (NN)
Microcytic hypochronic (MH)
Megaloblastic (MB)
Mixed

TABLE - 4

Sex wise distribution of microcytic hypochromic anemia

Number of cases of microcytic hypochromic anemia	Male		Female	
	No.	%	No.	%
13	4	30.7	9	69.21

Out of total 13 cases of microcytic hypochronic anemia, 4 cases were male and 9 were female. Thus in terms of percentage, out of all cases of microcytic hypochronic anemia, about 70% were female and 30% were male.


Sex wise distribution of microcytic hypochromic anemia
10
9
8
7
6
5
4
3
2
1
0
Male
Female

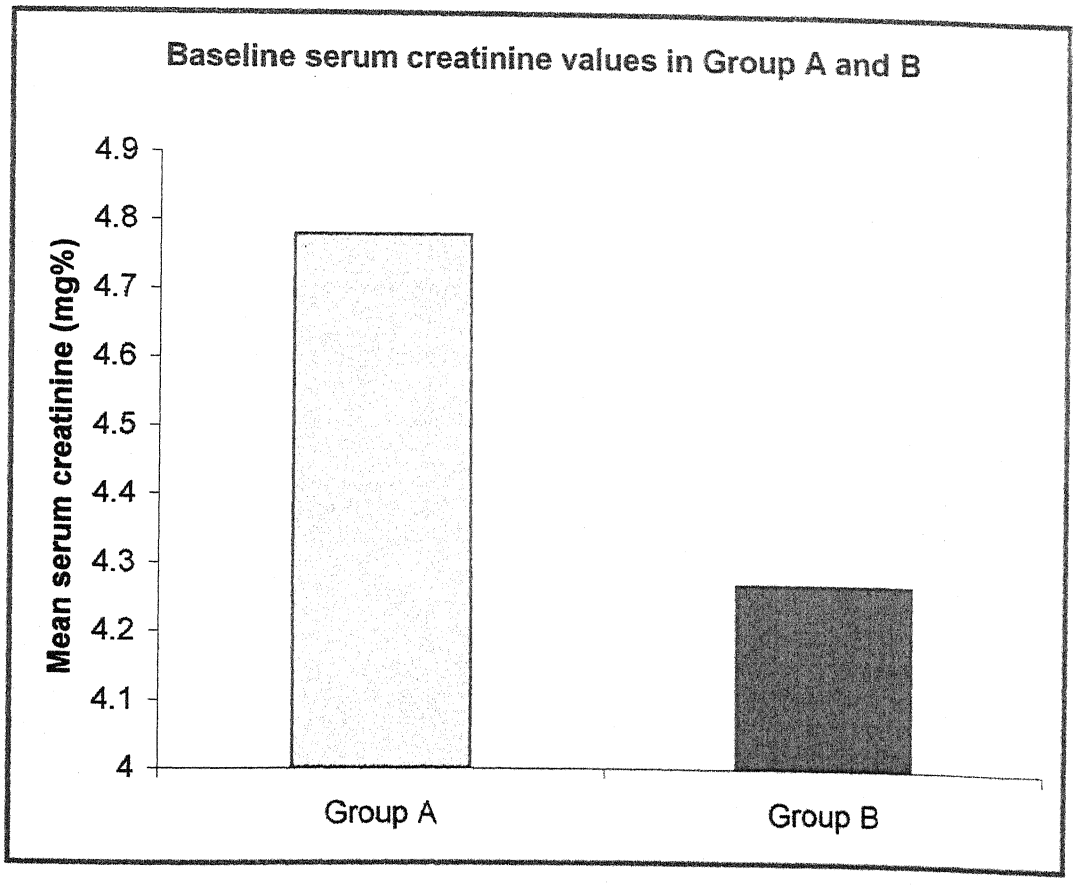

Baseline serum creatinine values in Group A and B
Mean serum creatinine (mg%)
4.9
4.8
4.7
4.6
4.5
4.4
4.3
4.2
4.1
4
Group A
Group B

TABLE – 6

Baseline hematological parameters in Group A and B

	Group A (mean±SD)	Group B (mean±SD)
Hemoglobin (gm%)	6.20±1.10	5.64±0.83
Hematocrit (%)	18.55±3.28	17.0±1.96

In Group A mean baseline hemoglobin was 6.20±1.10 and hematocrit was 18.55±3.28, whereas in Group B, mean baseline Hb was 5.6±0.83 and hematocrit was 17.0±1.96.

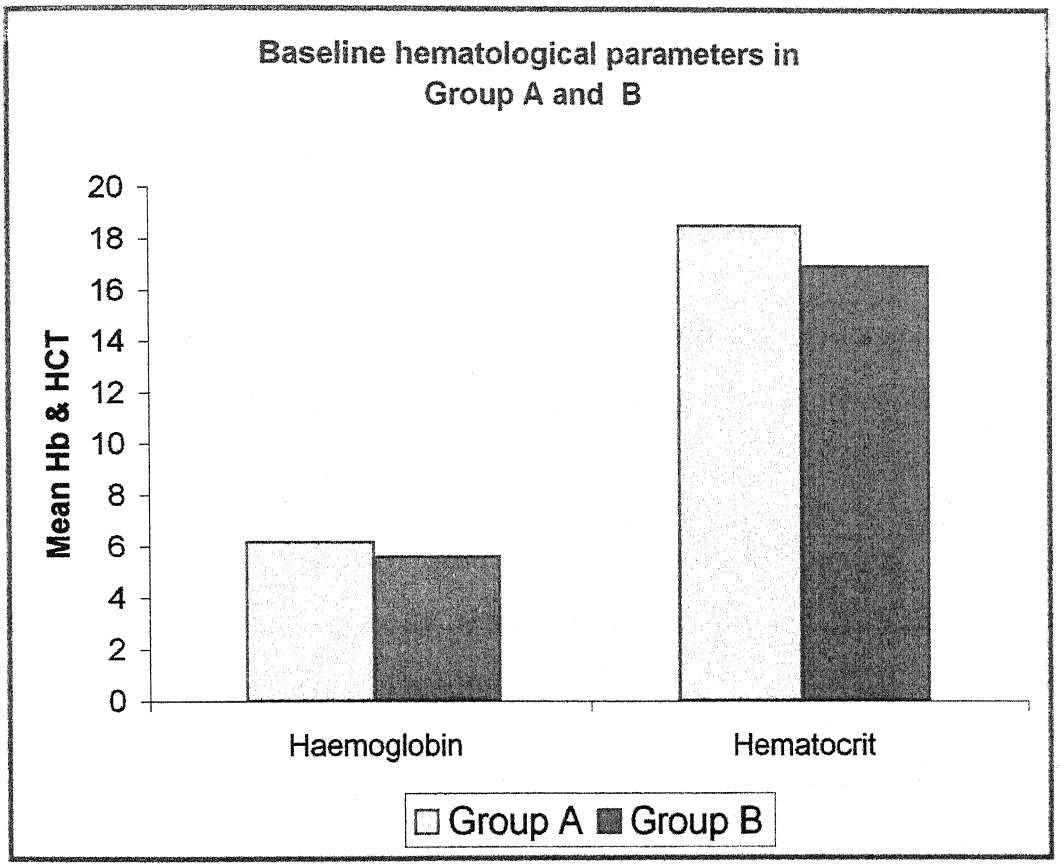

Baseline hematological parameters in
Group A and B
Mean Hb & HCT
20
18
16
14
12
10
8
6
4
2
0
Haemoglobin
Hematocrit
Group A
Group B

TABLE - 7

Effect of oral and I/V iron therapy on hemoglobin concentration

Group	Baseline Hb (gm%) (mean±SD) (a)	Hb at 1 month (gm%) (mean±SD) (b)	Hb at 2 month (gm%) (mean±SD) (c)	Hb at 3 month (gm%) (mean±SD) (d)	Pared P vaue (aVsd)	Unpaired P value (AvsB)
A	6.20±1.10	7.10±1.23	7.83±1.07	8.70±1.20	< 0.001	<0.001
B	5.64±0.83	7.03±1.0	8.67±0.93	10.42±1.20	< 0.001	

In patients of Group A, who were put on oral iron therapy, the mean hemoglobin level increased from a baseline value of 6.20±1.10 to 8.70±1.20 at the end of 3 months of therapy.

In patients of Group B, who were put on I/V therapy, the mean hemoglobin level increased from a baseline value of 5.64±0.83 to 10.42±1.20 at the end of 3 months of therapy.

It is clearly evident that there was significant increase in hemoglobin concentration in both the groups with 3 months of therapy ($P<0.001$) and the difference in hemoglobin rise between the two groups A and B was also statistically significant ($P<0.001$).

The rise in Hb level after the 3 months of iron therapy was more in Group B as compared to Group A, indicating a better response with I/V iron as compared to oral iron therapy.

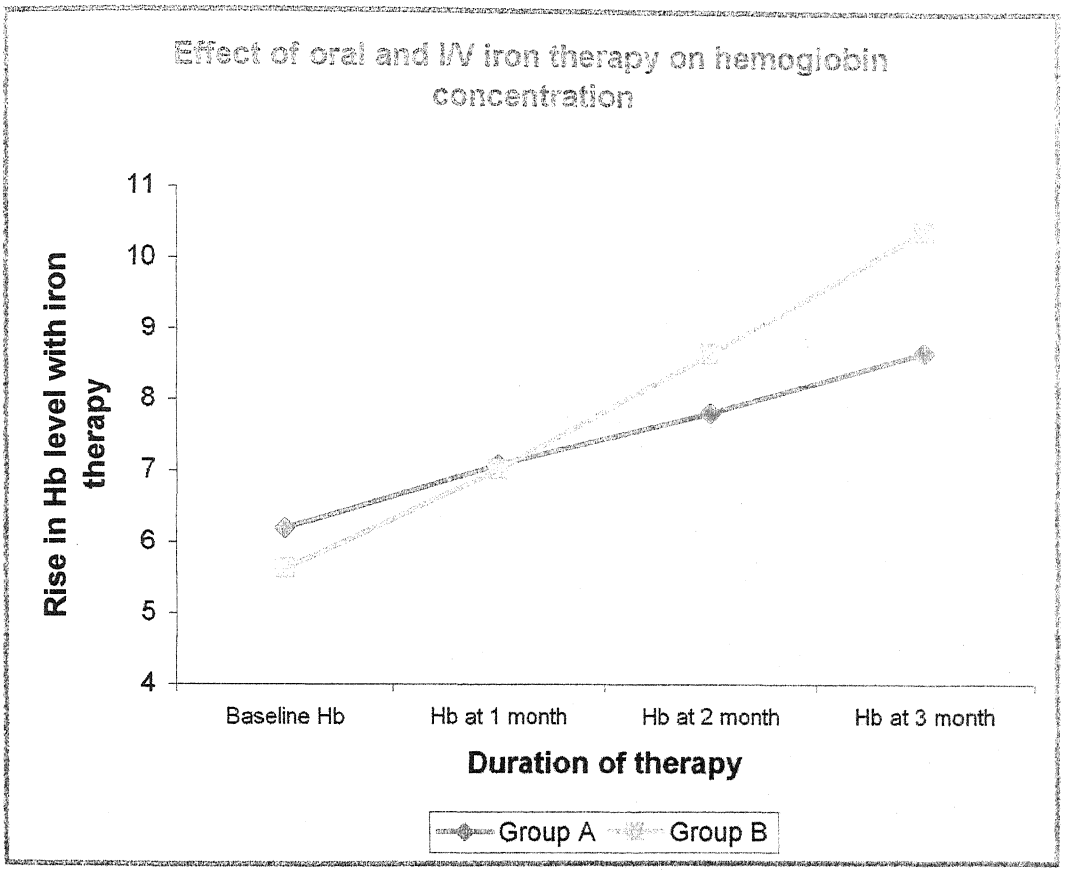

Effect of oral and I/V iron therapy on hemoglobin concentration
Rise in Hb level with iron therapy
11
10
9
8
7
6
5
4
Baseline Hb
Hb at 1 month
Hb at 2 month
Hb at 3 month
Duration of therapy
Group A
Group B

TABLE -8

Effect of oral and I/V iron therapy on hematocrit (Hct)

Group	Baseline Hct (%) (Mean±SD)	Hct at 3 months (%) (Mean±SD)	Paired p value	Unpaired p value
A	18.55±3.28	28.05±2.07	< 0.001	< 0.001
B	17.0±1.96	33.05±2.3	<0.001	

In patients of Group A, there was a rise of Hct from mean baseline value of 18.55±3.28 to 28.05±2.07 at the 3rd month of therapy that was statistically significant (P<0.001).

In patients of group B, there was a rise of Hct from the mean baseline value of 17.0±1.96 to 33.05±2.3 at the 3rd month of therapy and this was also significant (P<0.001).

The difference in Hct rise between the patients of Group A and B was also statistically significant (P<0.001).

As it is clear from the table, there is a more marked increase in Hct in patients of Group B, that shows a definite better response with I/V iron therapy as compared to oral iron therapy.

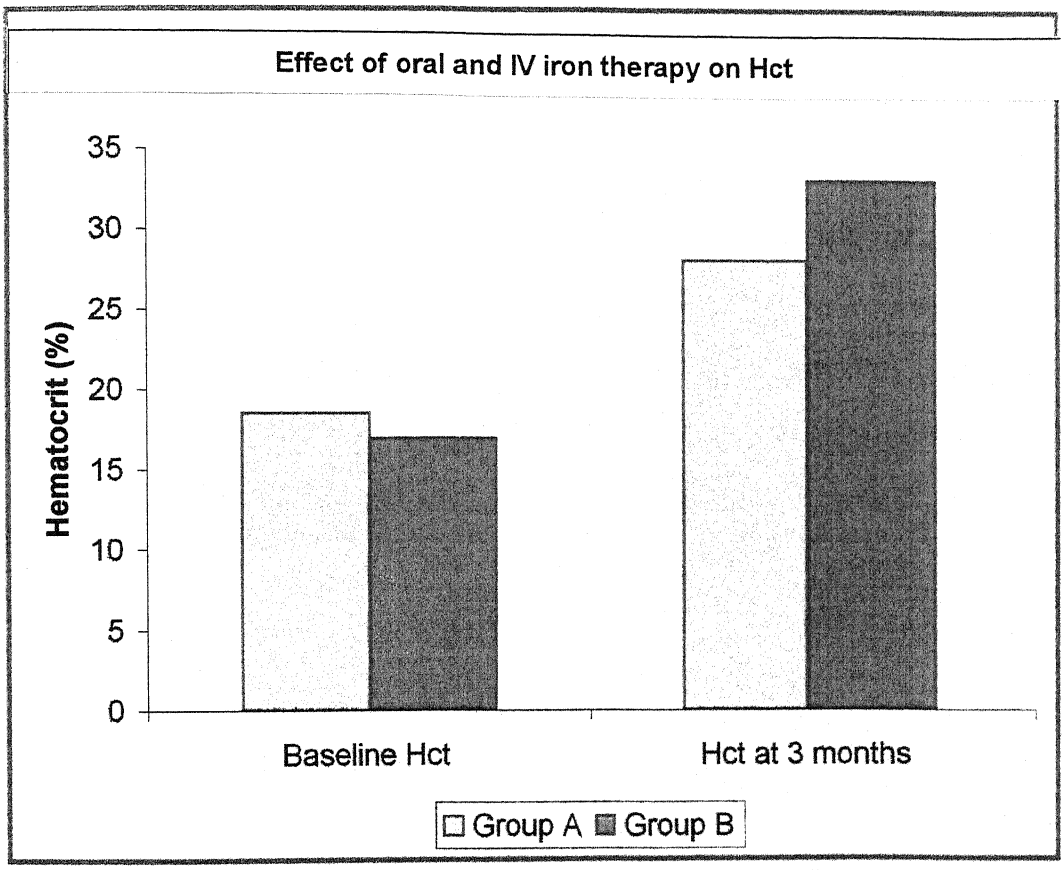

Effect of oral and IV iron therapy on Hct
Hematocrit (%)
35
30
25
20
15
10
5
0
Baseline Hct
Hct at 3 months
Group A
Group B

TABLE -9

Effect of oral and I/V iron therapy on serum iron

Group	Baseline serum iron (µg/dl) (Mean±SD) [a]	Serum iron at 3 months (µg/dl) (Mean±SD) [b]	Paired p value [a vs b]
A	103.6±19.0	79.85±21.72	< 0.001
B	99.35±20.22	113.7±21.57	<0.01

In Group A, there was a statistically significant decrease in serum iron from the baseline value of 103.6±19.0µg/dl to 79.85±21.72µg/dl at the end of 3 months of therapy (P<0.001). However in patients of Group B there was a statistically significant increase in serum iron from baseline value of 99.35±20.22µg/dl to113.7±21.57µg/dl with 3 months of therapy (P<0.01).

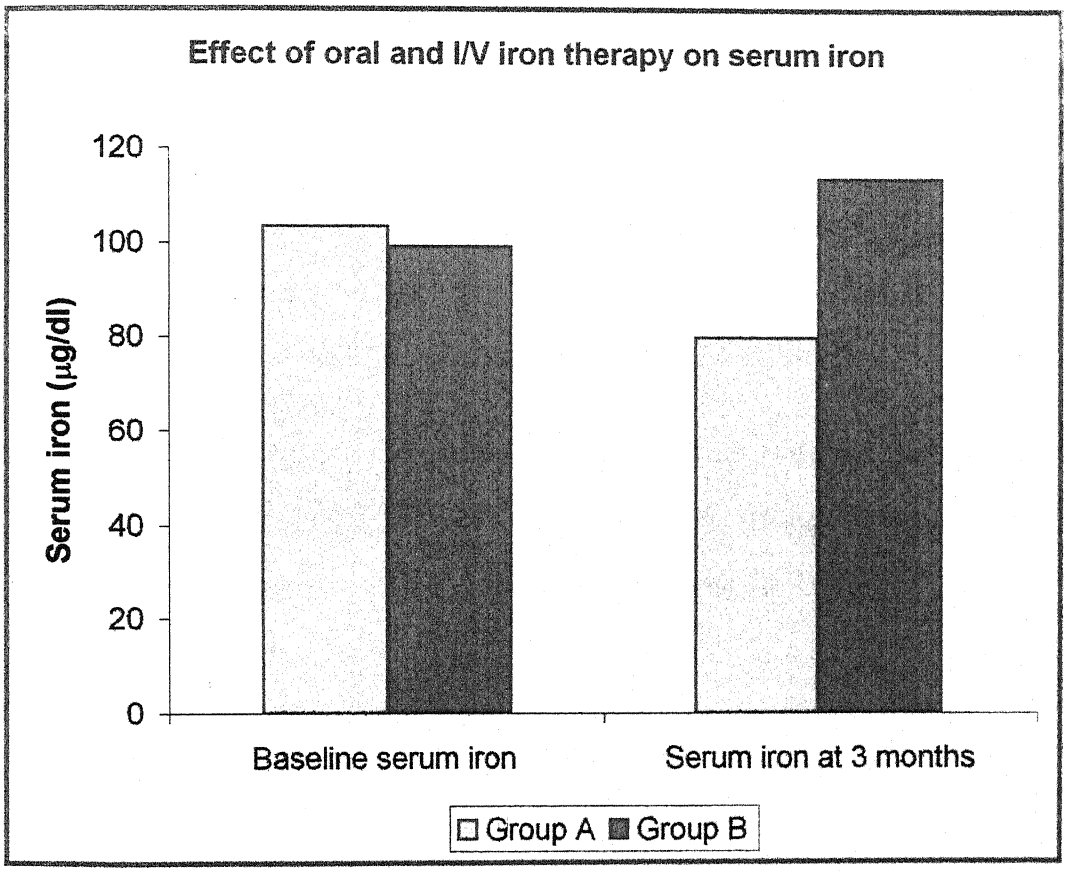

Effect of oral and I/V iron therapy on serum iron
Serum iron (µg/dl)
120
100
80
60
40
20
0
Baseline serum iron
Serum iron at 3 months
Group A
Group B

TABLE -10

Effect of oral and I/V iron therapy on serum ferritin

Group	Baseline serum ferritin (ng/ml) (Mean±SD) [a]	Serum ferritin at 3 months (ng/ml) (Mean±SD) [b]	Paired p value [a vs b]
A	156.8±33.20	95.9±29.52	< 0.001
B	153.85±29.70	216.55±32.46	<0.001

In patients of Group A, serum ferritin levels showed a statistically significant decrease from the baseline value of 156.8±33.20 to 95.9±29.52ng/ml with 3 months of iron therapy ($p<0.001$).

In patient of Group B, the serum ferritin level showed an increase from the baseline value of 153.85±29.70 to 216.55±32.46 ng/ml with 3 months of therapy and this was also statistically significant ($p<0.001$).

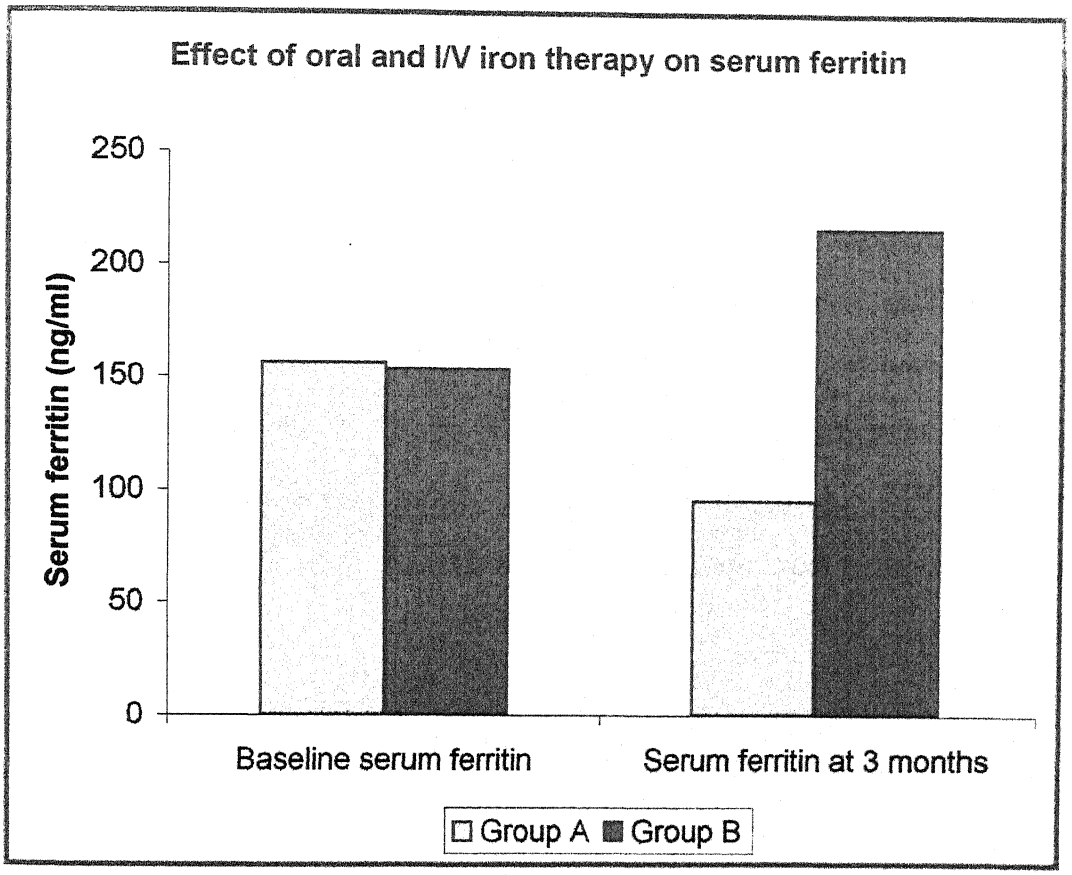

Effect of oral and I/V iron therapy on serum ferritin
Serum ferritin (ng/ml)
250
200
150
100
50
0
Baseline serum ferritin
Serum ferritin at 3 months
Group A
Group B

TABLE -11

Effect of oral and I/V iron therapy on total iron binding capacity (TIBC)

Group	Baseline TIBC (µg/dl) (Mean±SD) (a)	TIBC at at 3 months (µg/dl) (Mean±SD) (b)	Paired p value (a vs b)	Unpaired p value (A vs B)
A	253.55±27.12	242.75±29.0	> 0.05	> 0.05
B	256.80±31.75	238.7±28.70	>0.05	

In Group A, there was a statistically significant decrease in TIBC from the baseline value of 253.55±27.12 to 242.75±29.10 µg/dl with 3 months of therapy ($p<0.05$). In Group B also there was a statistically significant decrease from baseline value of 256.80±31.75 to 238.7±28.70. The decrease in TIBC was also significant when compared between the two groups ($p>0.05$).

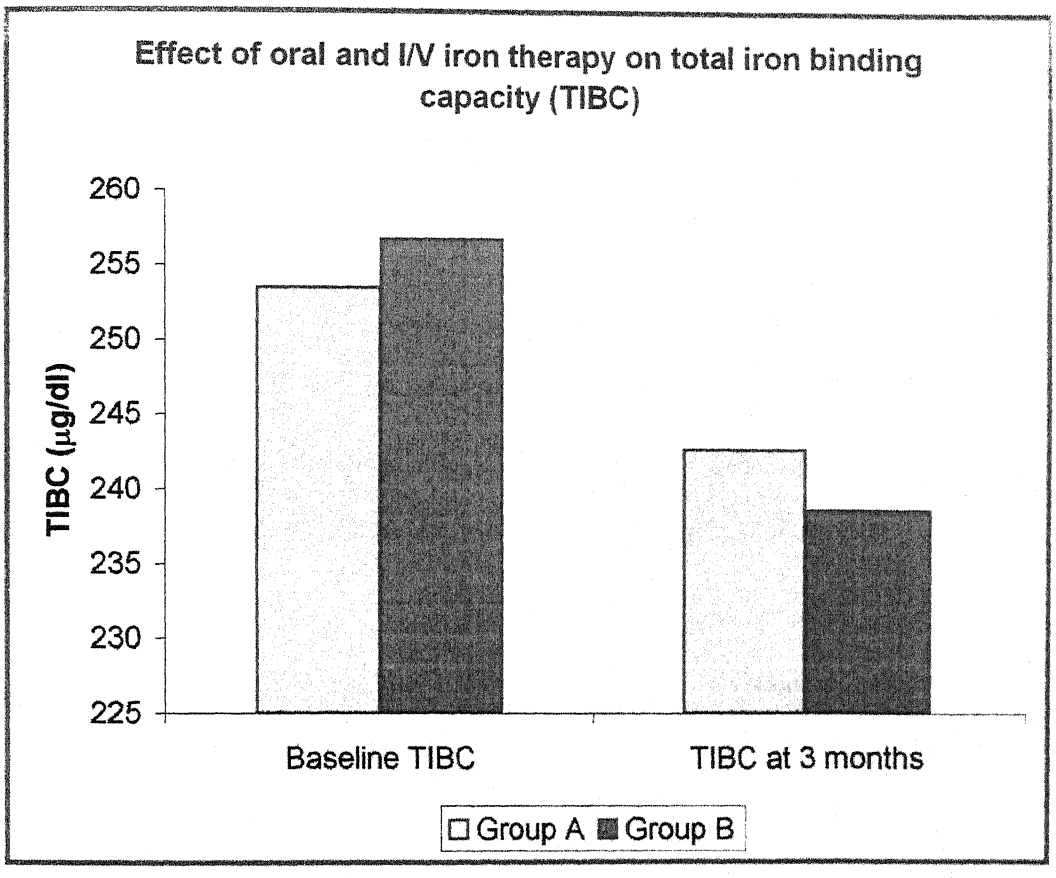

Effect of oral and I/V iron therapy on total iron binding capacity (TIBC)
TIBC (µg/dl)
260
255
250
245
240
235
230
225
Baseline TIBC
TIBC at 3 months
Group A
Group B

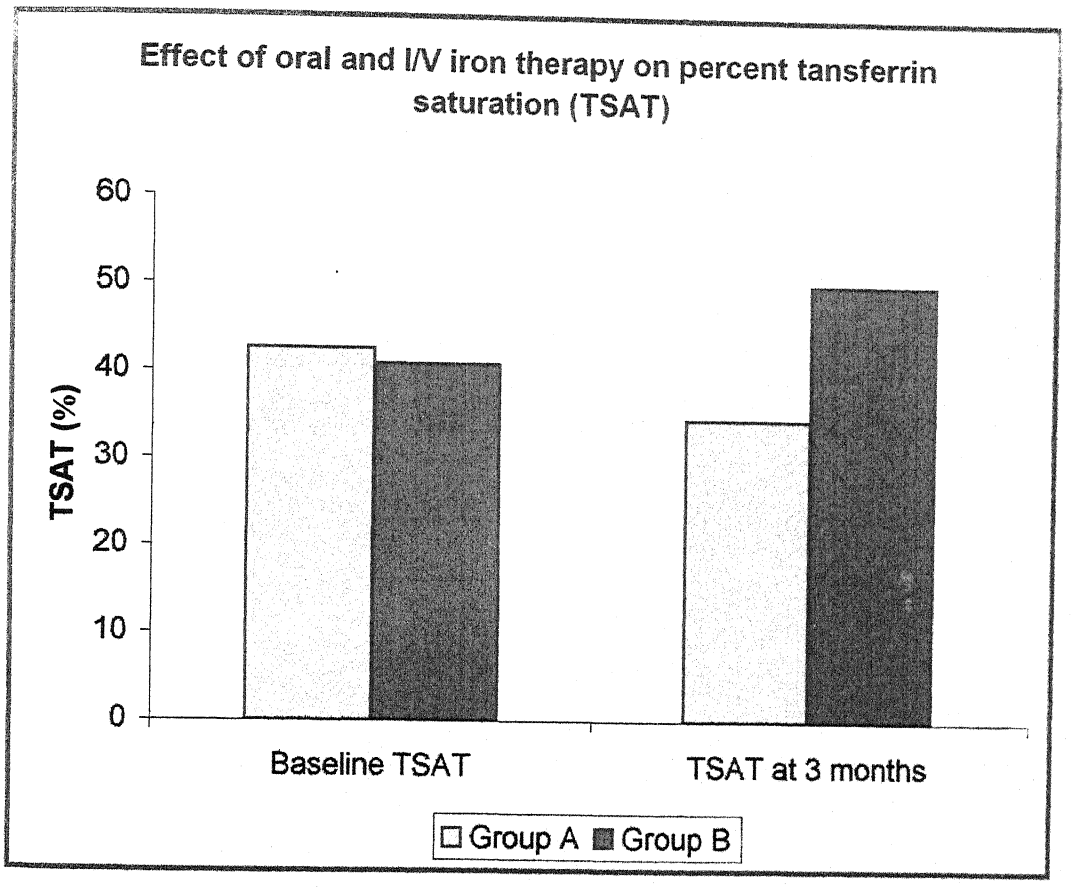
TABLE –12

Effect of oral and I/V iron therapy on percent tansferrin saturation (TSAT)

Group	Baseline TSAT(%) (Mean±SD) (a)	TSAT at 3 months (%) (Mean±SD) (b)	Paired p value (a vs b)	Unpaired p value (A vs B)
A	42.64±10.8	34.70±12.96	< 0.001	< 0.001
B	40.90±9.46	50.30±7.69	< 0.01	

In group A, there was a statistically significant decrease in TSAT from the baseline value of 42.64±10.8 to 34.70±12.96 at the 3 months of therapy. In Group B, there was a statistically significant increase in TSAT from the baseline value of 40.90±9.46 to 50.30±7.69 at the 3 months of therapy ($p<0.01$).

The difference between the two groups was also statistically significant ($p<0.001$).


Effect of oral and I/V iron therapy on percent tansferrin saturation (TSAT)
TSAT (%)
60
50
40
30
20
10
0
Baseline TSAT
TSAT at 3 months
Group A
Group B

Discussion

DISCUSSION

Chronic renal disease with progressive renal failure is almost always accompanied by moderate to severe degree of anemia, which in its most typical form is normocytic normochronic type of hypoproliferative anemia with low reticulocyte production index. The failure in the marrow proliferation is primarily the result of reduced erythropoietin response for the degree of anemia. However, it is not only the impaired production of eythropoietin that is responsible for anemia in CKD, but a number of other factors also contribute like reduced red cell life span, iron deficiency, folate and B_{12} deficiency, aluminium toxicity, marrow fibrosis resulting from hyperparathyroidism and blood loss, and depending upon which of these factors predominates, the nature of anemia may vary.

In Indian patients, majority have associated iron deficiency, and therefore a microcytic hypochronic blood picture in Indian CKD patients is not very unusual.

Initiation of eythropoietin therapy, by increasing the rate of erythropoiesis and subsequently iron demand, causes a further functional Iron deficiency state and therefore Iron supplementation becomes essential. Iron can be given orally or parenterally. However, there are certain limitations of oral Iron over parenteral Iron therapy. The present study was conducted with the aim to know which mode of iron supplementation is better in correction of anemia in CKD.

The present study was conducted on 40 adults patients with CKD and anemia, who were attending the OPD and wards of Department of Medicine, MLB Medical College, Jhansi. After carrying out all the relevant baseline investigation to asses the type of anemia, the patients

were put into two groups- A and B. The patients of Group A received oral Iron in the form of one capsule of 300mg of Ferrous Fumerate (containing 100mg of elemental Iron) twice daily and patients of Group B received intravenous Iron in the dosage of 100mg of elemental iron as iron sucrose once every week. The patients of both the group received recombinant human erythropoietin in the dosage of 2000units subcutaneously twice weekly. The patients of both the groups are followed for a period of 3 months and the hematological parameters at 3 months were compared with the baseline parameters to assess the response to 3 months of Iron therapy.

COMPOSITION OF STUDY GROUPS

In Group A, out of all the 20 patients, 13 were male and 7 were female, with a male female ratio of 1.85:1. These patients were in age group ranging from 23 to 66 yrs and of these 85% of the patients were in age range 20 to 49 yrs.

In Group B, out of all the 20 patients 15 were male and 5 were female with the male female ratio of 3:1. The age range was 24 to 68 yrs, and of these 80% were in age group of 20-49 yrs.

TYPE OF ANEMIA

Out of all the patients studied, 47.5% had a normocytic normochronic anemia and 32.5% had a microcytic hypochronic anemia. 5% of the patients had megaloblastic blood picture whereas 15% had a mixed type of anemia. The finding that majority of the patients had normocytic normochronic anemia is consistent with the classical knowledge that the anemia in CKD is usually of hypoprolifeative type with normocytic

normochronic blood picture and low reticulocyte production index. The finding that a substantial number of patients (32.5%) had a microcytic hypochronic anemia clearly reflects the high prevalence of Iron deficiency among Indian population. Another important finding observed in the study was that out of all the CKD patients showing microcytic hypochronic anemia, about 70% were female, further stressing that, iron deficiency is much more common among females as compared with males.

Around 5% patient had megaloblastic blood picture and this indicates the prevalence of folate and vitamin B_{12} deficiency.

RENAL PARAMETER

Serum creatinine was take as baseline renal parameter to assess the severity of renal impairment.

In this study patients of Groups A had a mean serum creatinine value of 4.78±1.89mg/dl and of Group B 4.27±1.62mg/dl, indicating the comparability of the two groups with respect to degree of renal impairment.

Means and Krantzy et al reported that as the blood urea nitrogen (BUN) approaches 100mg% and creatinine rises above 3 to 5mg/dl, the Hb level falls below 7mg/dl. Similar results were reported by Mertz and Koschnich et al. The findings observed in the present study are consistent with the findings of these workers, as the mean Hb level in the patients of Group A was 6.20±1.10 and in Group B 5.64±0.83; indicating the impact of renal impairment and raised serum creatinine.

HEMATOLOGICAL PARAMETERS

Hb level and Hct were taken as the hematological parameters to assess the severity of anemia as well as the response to Iron therapy.

Baseline Hb and Hct values were 6.20±1.10 and 18.55±3.28 in Group A and 5.64±0.83 and 17.0±1.96 in Group B.

EFFECT OF ORAL I/V IRON THERAPY ON HEMATOLOGICAL PARAMETERS

The patients of Group A were put on oral Iron therapy and their Hb values showed a continuous increase form above mentioned baseline mean values to 7.10±1.23 at 1 month, 7.83±1.07 at 2 months and 8.70±1.20 at 3 months of therapy, thus showing a net increase of 2.5gm/dl with 3 months of oral Iron therapy.

Likewise, the Hct values also shown a continuous increase form above mentioned baseline value to 28.05±2.07 at 3 months of therapy, showing a net increase of 9.5% with 3 months of oral Iron therapy.

The patients of Group B were put on I.V Iron therapy and their Hb level increased from above mentioned baseline mean value to 10.42±1.20 at 3 months of therapy, showing a net increase of 4.78gm/dl. Similarly their Hct values also increased from baseline mean value of 17.0± 1.96 to 33.05±2.3 at 3 months of I/V Iron therapy, showing a net increase of 16.05%.

Thus, it is evident from this study that rise in Hb level as well as Hct value is much more in Group B as compared to Group A, clearly indicating a much better response to I.V Iron therapy as compared to oral Iron therapy in terms of improvement in haematological parameters.

The poor response to oral Iron therapy as compared to I/V Iron therapy has been attributed to a number of factors, the most important being inadequate iron absorption form the gut coupled with poor patient compliance due to inconvenient dosing schedule and side effects of oral Iron like gastric irritability.

Various studies have confirmed that although a rise in Hb level and Hct is achieved in all CKD patients put on oral Iron therapy but the response is usually inadequate, especially when these patients are receiving erythropoietin which greatly stimulates marrow erythropoiesis and creates a further functional iron deficiency. By giving I.V Iron in a proper dosing schedule these patients can be optimally benefited. A state of positive Iron balance can be achieved in which there is sufficient Iron available for erythropoiesis and adequate Iron stores can be established.

Silverberg DS et al, based on their own studies, advocated the use of I.V Iron therapy and clearly showed the superiority of I/V Iron over oral Iron supplementation in correction of anemia in CKD patients, both in terms of rise in Hb and Hct levels as well as in establishing adequate Iron stores. They also found that, these patients who were put on I/V iron therapy required a relatively reduced dosage of erythropoietin to achieve target Hb and Hct levels, and this is another advantage of maintaining adequate Iron stores with I/V Iron.

Another study conducted by ***Ahsan N (1998)*** compared the use of I/V iron with oral Iron in correction of anemia in CKD patients who were put on peritoneal dialysis and this also proved the higher efficacy of I/V Iron over oral Iron. These workers also found that single I/V infusion of total

dose Iron is a safe and well tolerated method of Iron administration that can be used on out patient basis.

Agarwal HK and co-workers (2002) also performed a similar study comparing the efficacy of I.V iron with oral Iron in predialysis CKD patients put on erythropoietin therapy and further established the superiority of I/V Iron.

The results obtained form our study are similar to those of these workers showing a much better response to I/V Iron than oral Iron in raising the Hb and Hct values with the similar dosage of erythropoietin. The rise in Hb and Hct values with the 3 months therapy with I.V Iron is much greater in our study as compared with earlier studies, and this can be attributed to the use of a newer more potent form of I/V Iron – Iron sucrose that was used in our study. ***Agarwal and co-workers*** used Iron dextran. And thus another conclusion that can be drawn from our study is a better response from Iron sucrose as compared with iron dextran when used with similar dosage of erythropoietin.

EFFECT OF ORAL AND I/V IRON THERAPY ON FERROKINETIC PARAMETERS

Ferrokinetic studies provide a valuable tool in establishing the Iron status of an anemic patient and monitoring the response to the therapy. These studies have provided a dramatic improvement in the management of anemia in CKD patients. The diagnosis, treatment as well as monitoring the response to the treatment all are based on values of these ferrokinetic parameters and the guidelines issued for the treatment of renal anemia are directed on these parameters. These parameters include serum iron level that reflect the overall level of circulating Iron, Serum Ferritin level that

reflects Iron stores, percent transferrin saturation and total Iron binding capacity that represent the amount of Iron being transported by transferrin and further capacity of transferrin to bind Iron, respectively. Of these the two most important ones are serum ferritin and percent transferrin saturation and the guidelines issued by National Kidney Foundation (NKF-K/DOQI) recommended that in order to achieve and maintain a target Hb of 11-12gm/dl and Hct of 33-36%, sufficient Iron should be administered to the patient so as to maintain the % transferring saturation ≥20% and serum ferritin ≥100ng/dl.

In our study we took all the four ferokinetic parameters for evaluation of response to Iron therapy. Ferrokinetic studies were performed in all the patients of group A and B, once before initiation of Iron therapy and then again at the time of completion of 3 months of therapy. All the four parameters were compared between the patients of both the groups.

EFFECT OF ORAL AND I/V IRON THERAPY ON SERUM IRON

There was a significant decrease in serum Iron from a mean baseline value of 103.6±19.0 to 79.85±21.72 at the end of 3 months of Iron therapy in patients of Group A ($p<0.001$). Whereas in patients of Group B who received I/V Iron a significant increase ($p<0.01$) in serum Iron was observed form a base line value of 99.35±20.22 to 113.7±21.57 at the end of 3 months of therapy.

The significant decrease in serum Iron in patients of Group A who were treated with oral Iron clearly shows the effect of erythropoietin. The administration of errythropoietin in CKD patients greatly enhances the rate of erythropoiesis, upto several folds, thus significantly increasing the

Iron requirement of these patients and if this requirement is not met, the patients become more and more Iron deficient with a resultant fall in serum iron levels and depletion of iron stores. As it is clear form our results, despite of administration of oral Iron, the serum Iron levels falls, showing that oral iron therapy is insufficient in meeting this increased iron demand. The patients of Group B, who received the same dosage of erythropoietin but were put on I/V Iron showed a significant rise in serum Iron, in addition to a higher increase in Hb and Hct values. This observation clearly shows the superiority of I/V Iron over oral iron in treatment of renal anemia in CKD patients, put on erythropoietin therapy.

These findings are consistent with the work of ***Agarwal HK et al (2002)***, who also observed a similar fall in the serum iron with oral iron and rise with I/V Iron.

EFFECTS OF ORAL AND IV IRON THERAPY ON SERUM FERRITIN

In patients of Group A there was a significant decrease in serum ferriitin from a baseline value of 156.8±33.20 to 95.9±29.52 at 3 months of therapy, where as in Group B there was a significant increase from baseline value of 153.85±29.70 to 216.55±32.46 at 3 months.

The fall in serum ferritin in the patients of Group A, who were put on oral Iron therapy shows increased mobilization of marrow iron stores as the oral iron is insufficient to meet the increased iron requirement due to erythropoeitin administration. The patients of Group B who received I.V iron showed an increase in serum ferritin, meaning thereby building up of Iron stores as the I/V Iron can provide sufficient Iron for erythropoeitin as well as for creating a positive Iron balance.

These findings are consistent with the work of ***Svara F et al (1996)*** who also observed a similar fall in serum ferritin in the patient, treated with the oral Iron and erythropoietin.

EFFECT OF ORAL AND I/V IRON ON TIBC

In patients of Group A, a significant ($p>0.05$) decrease in TIBC was observed from a mean baseline value of 253.55±27.12 to 242.75±29.0 at the end of therapy. In Group B also there was a significant decrease ($p>0.05$) from baseline value of 256.80±31.75 to 238.7±28.70.

In chronic kidney disease with anemia, TIBC usually does not change too much. As the Iron therapy increases % transferrin saturation, a fall is observed in TIBC with the beginning of Iron therapy.

EFFECT OF ORAL AND I/V IRON ON PERCENT TRANSFERRIN SATURATION [TSAT]

In Group A, a significant ($p<0.001$) fall was observed in TSAT value from a mean baseline value of 42.64±10.8 to 34.70±12.96 at 3 months of therapy, whereas in Group B a significant ($p<0.01$) rise was seen from mean baseline value of 40.90±9.46 to 50.30±7.69. The difference between Group A and B was also found to be statistically significant.

The observations clearly show the better response with I/V iron as compared with oral iron in treatment of anemia with CKD. These findings are consistent with the work of ***Agarwal HK et al (2002)*** who also observed a similar fall in TSAT with oral Iron and increase with I/V Iron.

Thus our study clearly establishes that the I/V Iron is a better mode of therapy than oral Iron in treatment of anemia in patients with CKD who

are put on erythropoietin. The rise in Hb and Hct levels as well as improvement in ferrokinetic parameters showing stored Iron and Iron available for erythropoiesis was found to be much better in the patient group receiving I/V Iron. Also the newer I/V iron preparation, iron sucrose, that we used in our study was found to be extremely safe and effective and we did not observe any case of anaphylaxis during our study.

Summary & Conclusions

SUMMARY AND CONCLUSIONS

1. The study was undertaken on forty adult patients of CKD with anemia coming to OPD and wards of Department of Medicine, MLB Medical College, Jhansi. All the patients who were enrolled in the study were advised necessary base line investigations to look for renal and hematological parameter.

2. On the basis of hematological parameters, type of anemia was established.

3. The patients were randomly put into two groups A and B each consisting of 20 patients. Patients of Group A were given oral Iron in the form of one capsule of 300mg of Ferrous fumerate (containing 100mg of elemental iron) twice daily. The patients of group B were given 100mg of elemental iron in the form of Iron sucrose as I.V preperation per week.

4. Patients of both the groups were given recombinant human erythropoietin in the dosage of 2000 units subcutaneously twice weekly.

5. The patients were followed for a period of 3 months and at the end of 3 months of therapy the patients were reassessed for hematological parameters. The response to iron therapy was judged in terms of improvement in hematological parameters and the two groups were compared with each other.

6. The age range of patients in Group A was 23-66 years and in Group B was 24-68 years. In Group A 85% of the patients were in

age group 20-49 years where as in Group B 80% of the patients were in age group 20-49 years.

7. In Group A, 13 patients were male and 7 were female, where as in Group B, 15 were male and 5 were female. Thus male : female ratio in Group A was 1.85:1 and in Group B was 3:1.

8. Out of all the 40 patients studied, 47.5% had normocytic-normochromic anemia and 32.5% had microcytic hypochromic anemia. Megaloblastic anemia was observed in 5% cases whereas remaining 15% had a mixed type of blood picture. Out of all cases of microcytic hypochronic anemia 70% were females.

9. Mean baseline serum creatinine value was 4.78±1.89 in Group A and 4.27±1.62 in Group B.

10. In group A, mean baseline Hb was 6.20±1.10 and Hct was 18.55±3.28 and in Group B, Hb was 5.64±0.83 and Hct was 17.0±1.96.

11. In patients of Group A who were put on oral iron therapy, the mean Hb level increased from the baseline value of 6.20±1.10 to 8.70±1.20 and Hct increased from 18.55±3.28 to 28.05±2.07 with 3 months of therapy. Rise in both these value was statistically significant ($p<0.001$).

12. In patients of Group B, treated with I/V Iron, the rise in mean Hb level was from baseline value of 5.64±0.83 to 10.42±1.20 and in Hct from 17.0±1.96 to 33.05±2.3. This was also statistically significant ($p<0.001$).

13. Thus, in comparison, the rise in Hb as well as in Hct was much more in patients of Group B who received I/V iron therapy and the difference between the two groups was also statistically significant ($p<0.001$).

14. The increase in serum Iron was observed in patients of Group B who had a mean baseline level of 99.35±20.22 µg/dl and at 3 month 113.7±21.57 µg/dl and this was statistically significant ($p<0.01$). Contrary to this patients of Group A showed a statistically significant ($p<0.001$) fall in serum iron from a baseline level of 103.6±19.0 to 79.85±21.72 µg/dl at 3 months.

15. In patients of Group A, Se. ferritin value decreased significantly ($p<0.001$) from mean baseline value of 156.8±33.20 to 95.9±29.52 ng/ml at 3 months, whereas in patients of Group B, it increased significantly ($p<0.001$) from 153.85±29.70 to 216.55±32.46 ng/ml at 3 months.

16. TIBC in Group A decreased from 253.55±27.12 at baseline to 242.75±29.0 at 3 months and in Group B, from 256.80±31.75 at baseline to 238.7±28.70 at 3 months and both of these were statistically significant ($p>0.05$).

17. A statistically significant ($p<0.001$) fall was observed in TSAT in patients of Group A from baseline value of 42.64±10.8 to 34.70±12.96 at 3 months of therapy. Contrary to this a statistically significant ($p<0.01$) increase was observed in patients of Group B from baseline of 40.90±9.46 to 50.30±7.69 at 3 months.

Thus, it can be concluded from our study that –

1. Anaemia in majority of CKD patients in although of normocytic normochronic type, a reasonably high number of patients also have a microcytic hypochronic type.

2. I/V iron therapy is far better than oral Iron in management of anemia in CKD patients receiving erythropoietin.

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Appendix

MASTER CHART [GROUP - A]

Pt. No.	Age (yrs)	Sex	Type of Anemia	Serum Creat. (mg%)	Hb (gm/dl)				Hct (%)		S. Iron (µg/dl)		Se. ferritin (ng/ml)		TIBC (µg/dl)		TSAT (%)	
					0 mth	1 mth	2 mth	3 mth	0 mth	3 mth	0 mth	3 mth	0 mth	3 mth	0 mth	3 mth	0 mth	3 mth
1.	40	M	NN	1.6	7.8	8.6	9.3	10.1	23	34	154	128	204	140	208	198	70.03	64.64
2.	64	F	MB	5.6	6.3	7.1	7.7	9.0	19	28	140	114	201	131	223	216	62.78	52.77
3.	28	F	MH	3.6	7.2	8.0	8.7	9.4	22	28	52	44	102	60	298	289	17.44	15.22
4.	34	M	NN	3.4	6.7	7.6	8.3	9.0	19	27	144	110	198	108	220	208	65.45	52.88
5.	23	M	MIX	8.0	4.8	5.7	6.2	7.3	14	24	100	76	158	86	263	253	38.02	30.03
6.	36	M	NN	2.6	6.2	7.3	8.0	8.9	20	30	138	103	204	139	234	221	58.97	46.60
7.	42	M	NN	6.4	6.3	7.3	8.0	8.8	20	28	142	124	200	131	214	205	66.35	60.48
8.	32	F	MH	8.0	5.3	6.2	7.0	7.8	16	24	49	39	96	51	306	297	16.01	13.13
9.	28	M	NN	4.7	5.6	6.5	7.6	7.8	16	23	104	81	160	92	236	223	44.06	36.32
10.	44	M	MIX	6.6	5.5	6.3	7.2	8.0	17	26	121	93	188	124	260	251	46.53	37.05
11.	24	M	NN	6.2	4.9	5.9	6.4	7.7	14	23	130	103	197	120	241	230	53.94	44.78
12.	30	M	NN	2.3	6.8	7.6	8.4	9.5	20	30	138	111	201	133	227	215	60.79	51.62
13.	45	F	MIX	4.5	5.4	6.4	7.2	7.7	16	27	101	76	167	87	261	249	38.69	30.52
14.	66	M	MH	3.4	6.4	7.5	8.2	9.2	20	29	68	42	100	54	286	276	23.77	15.21
15.	29	M	NN	4.0	5.9	6.7	7.6	8.4	18	30	112	70	152	80	252	239	44.44	29.28
16.	33	M	NN	8.0	5.9	6.8	7.3	8.0	17	26	120	92	192	119	246	237	48.78	38.81
17.	31	F	MH	4.6	6.7	7.8	8.6	9.1	20	31	56	41	91	50	288	279	19.44	14.69
18.	29	F	MH	4.6	6.2	7.2	7.9	9.1	18	29	52	39	90	69	292	276	17.80	14.13
19.	63	M	MH	4.0	7.8	8.6	9.3	10.4	22	36	59	43	93	60	276	263	21.37	16.34
20.	41	F	MIX	4.2	6.3	7.2	7.7	8.8	20	28	92	68	142	84	240	230	38.33	29.56
					6.20	7.10	7.83	8.70	18.55	28.05	103.6	79.85	156.8	95.9	253.55	242.75	42.64	34.70

MASTER CHART [GROUP - B]

Pt. No.	Age (yrs)	Sex	Type of Anemia	Serum Creat. (mg%)	Hb (gm/dl)				Hct (%)		S. Iron (µg/dl)		Se. ferritin (ng/ml)		TIBC (µg/dl)		TSAT (%)	
					0 mth	1 mth	2 mth	3 mth	0 mth	3 mth	0 mth	3 mth	0 mth	3 mth	0 mth	3 mth	0 mth	3 mth
1.	26	F	MH	7.0	4.2	5.6	7.2	9.0	12	28	37	52	71	144	306	288	12.09	18.05
2.	52	M	NN	3.6	6.6	8.0	9.6	11.1	20	35	132	145	204	270	228	212	57.89	68.39
3.	31	M	NN	4.0	5.0	6.3	8.0	10.0	15	32	110	127	190	251	242	223	45.45	56.95
4.	39	M	MIX	3.6	6.3	7.8	9.2	10.8	19	33	104	123	178	248	256	240	40.62	51.25
5.	32	M	NN	3.7	6.2	7.6	9.2	11.2	19	34	138	151	201	280	230	210	60.00	71.90
6.	40	M	NN	4.6	5.1	6.4	8.2	9.8	16	30	126	140	190	257	246	230	51.21	60.86
7.	61	M	MH	5.0	5.1	6.5	8.1	10.0	15	31	67	82	80	153	286	267	23.42	30.71
8.	28	F	MH	4.2	4.7	6.1	7.7	9.3	14	28	44	59	76	149	294	276	14.96	21.37
9.	57	M	MB	6.8	5.3	6.7	8.3	10.3	16	36	139	150	210	269	218	203	63.76	73.89
10.	32	M	NN	4.0	5.5	6.9	8.5	10.1	17	35	123	136	200	283	236	215	52.11	63.25
11.	24	M	NN	3.6	6.9	8.3	9.9	11.9	21	38	142	158	214	279	218	199	65.13	79.39
12.	27	M	NN	8.4	4.8	6.2	7.8	9.6	14	29	100	116	180	254	263	146	38.02	79.45
13.	33	F	MH	4.2	5.2	6.6	8.2	9.8	16	32	38	54	70	131	308	289	12.33	18.68
14.	46	M	MIX	3.4	6.0	7.4	9.2	11.0	18	34	101	116	182	144	250	232	40.40	50
15.	68	M	MH	5.7	4.9	6.5	8.3	9.7	15	31	62	74	79	130	280	260	22.14	28.46
16.	45	M	NN	3.4	5.3	6.7	8.5	9.9	16	32	104	117	170	224	261	242	39.84	48.34
17.	36	F	MH	2.0	5.9	7.2	9.0	10.7	17	35	50	63	69	132	298	281	16.77	22.41
18.	46	M	NN	2.9	6.4	7.5	9.1	11.0	20	34	158	172	220	290	204	285	77.45	60.35
19.	27	M	NN	3.4	5.8	7.2	8.8	10.8	17	35	138	153	201	267	242	224	57.02	68.30
20.	36	F	MH	2.0	7.6	9.1	10.7	12.4	23	39	74	86	92	176	270	252	27.40	34.12
					5.64	7.03	8.67	10.42	17	33.05	99.35	113.7	153.85	216.55	256.8	238.7	40.90	50.30